REMARKS

This document is filed in reply to the Office Action dated August 27, 2003 ("Office Action"). As suggested by the Examiner, Applicants have amended the Abstract of the application. Applicants have also amended claim 1 to include the limitation recited in original claim 7, necessitating the cancellation of claim 7 and the dependency change of claim 8. Applicants have also amended claims 1-6, 8-9, 11-12, and 20-21 to promote clarity. No new matter has been introduced.

Claims 1-6 and 8-21 are pending. Claims 13-19 have been withdrawn from further consideration for being drawn to a non-elected invention. Claims 1-6, 8-12, and 20-21 are now under examination. Reconsideration of this application is requested in view of the following remarks:

Objections to specification and claims

The Examiner objected to the Abstract and claims 1-9, 11-12, and 20-21 for informalities. Applicants have amended the Abstract, cancelled claim 7, and amended the other rejected claims. It is submitted that these amendments have overcome the objections.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 2, 4, and 6-8 as being indefinite. See page 3, lines 22-24, and page 4, lines 4-15. In view of the amendments to these claims, Applicants submit that the rejections have been overcome.

The Examiner also rejected claims 3 and 5 as being indefinite, alleging that the phrase "derived from" recited in these claims is vague . See the Office Action, page 4, lines 1-3.

Applicants disagree. Claim 3 is drawn to a retroviral expression vector. The vector contains the LTR region, the U3 region, or the R and U3 regions derived from a human endogenous retroviral nucleotide sequence. Applicants would like to point out that "a [Y] region derived from a [X] nucleotide sequence" is synonymous to "a [Y] region in a [X] nucleotide sequence;" that is, a Y region (e.g., the LTR region) from the X nucleotide sequence. See, e.g.,

the specification, page 9, first paragraph. In other words, one skilled in the art would clearly understand what "a region ... derived from a human endogenous retroviral nucleotide sequence" means. Claim 5 covers a retroviral expression vector containing a cell-specifically controllable promoter region that "is derived from the LTR region of a cell-specifically expressed endogenous human retroviral nucleotide sequence." For the same reasons set forth above, one skilled in the art would understand the meaning of the phrase "derived from" recited in this claim. Thus, Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-4, 6-13, and 15 for lack of enablement on various grounds. See page 3, lines 13-15. Applicants address each ground below:

It is the Examiner's position that the vector of the claims is not credible. More specifically, the Examiner asserted that:

> The claims read on using the claimed retroviral expression vectors or retroviral vector system for gene therapy in vivo in light of the specification ... The specification ... fails to provide adequate guidance for the correlation between the cell-specific expressed gene product and a particular disease or disorder.

Applicants would like to point out that "[i]f reasonably correlated to the particular therapeutic or pharmacological utility, data generated using ***in vitro*** assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process" (emphases added). See the MPEP, 2107.02III. Thus, if reasonably correlated to an asserted particular utility, *in vitro* data **alone** is sufficient.

In this connection, the Specification provides *in vitro* examples showing that the expression vectors of this invention possess the abilities to cell-specifically express a desired gene product. See, e.g., page 17 line 15 through page 20, line 27of the Specification. Further, the Specification has cited a number of references that teach how to use retroviral expression vectors for expression of desired genes. See, e.g., Price et al., 1987; Salmons et al., 1993; Schulte et al., 1996; and Ting et al., 1992. Applicants would also like to bring to the Examiner's

attention four referecens, i.e., Blaese et al., 1995, Science 270: 475-480; Grossman et al., 1994 Nat. Genet.6 (4): 335-341; Bordignon et al., 1995, Science 270:470-474; and Gunzburg et al., 1996, J. Mol. Med. 74(4):171-82, copies of which are attached hereto as Exhibits A, B, C, and D, respectively. These references teach how to use retroviral expression vectors for cell-specific expression of adenosine deaminase and LDL receptor, both of which are sufficiently present at target sites to provide therapeutic effects for adenosine deaminase deficiency and hypercholersterolaemia in vivo via various administration routes. In view of the teachings from the Specifcaiton and common knowledge in the art, Applicants sumbitt that the claims at issue are enabled.

For the reasons set forth above, Applicants have presented relevant data sufficient enough to establish a reasonable correlation between the activity of a claimed vector and its asserted utility. The invention is therefore credible and the Specification has met the enablement requirement.

It is also the Examiner's position that "the state of the prior art [in gene therapy] was not well developed and was highly unpredictable at the time of filing." To support this position, the Examiner relied on four references, which list several important factors for and obstacles to successful gene therapy. The Examiner then concluded that "it would require undue experimentation" for one skilled in the art to practice the invention. See the Office Action, page 6, line 5 through page 7, line 16.

Applicants note that the four references relied on by the Examiner point out many factors important to successful gene therapy. Nonetheless, they do not support the Examiner's position that "the state of the prior art was not well developed and was highly unpredictable at the time of filing." To the contrary, before the filing of this application, retroviral vectors had been successfully used in gene therapy for treating various diseases, including the adenosine deaminase deficiency and hypercholersterolaemia. See Blaese et al., 1995; Grossman et al., 1994; Bordignon et al., 1995; and Gunzburg et al., 1996 attached hereto (Exhibits A, B, C, and D, respectively). Furthermore, **a gene therapy has already been approved for treating head and neck squamous carcinoma**. See Nat. Biotech. 2004, 22: 3-4, a copy of which is attached

hereto as Exhibit E. The clinic trial for this gene therapy started in 1998, well before the filing of this application. Thus, at the time of this application was filed, the state of the prior art was sufficiently developed and was not highly unpredictable.

Incidentally, Applicants agree that obstacles (e.g., difficulty in tissue-specifically expressing a desired gene product) exist in gene therapy. Nonetheless, the application teaches how to overcome one such obstacle. That is, to achieve tissue specific expression of a desired gene product by taking advantage of HERV promoters, which are differentially active in human tissues. See, e.g., page 5, line 10 through page 7, and line 2.

In view of above remarks, Applicants submit that the claims at issue meet the enablement requirement.

Rejection under 35 U.S.C. § 103(a)

The Examiner only rejected claims 1-6, 10-12, 20, and 21 for obviousness over Verma et al. 1997 in view of Masahiro et al. and Sjottem et al. 1996. See the Office Action, page 8, lines 6-9. In other words, the Examiner has found that claims 7-9 to be free of prior art. Applicants have amended independent claim 1 to include the limitation recited in claim 7 and submit that amended claim 1, as well as claims 2-6,10-12, 20, and 21 (all including the limitation of claim 1), is patentable over the cited references as it now includes the art-free subject matter recited in claim 7.

CONCLUSION

Applicants submit that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is definite, enabled, and non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Enclosed is a $950 check for the Petition for Three Month Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket 10737-006001.

Respectfully submitted,

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